withdrawn as a result of a restriction requirement. However, Applicants previously elected Group I, claims 1-14, *26 and 35-37*. Correction is respectfully requested.

In the afore-referenced Action, Claims 1-11 and 13 stand rejected under 35 U.S.C. § 103(a) as being obvious over U.S. Patent No. 4,377,572 to Schwarz et al. ("Schwarz") in view of WO 92/13495 to Tripodi ("Tripodi"). Applicants respectfully assert that the present claims and remarks obviate this rejection.

Applicants claims are directed to therapeutic compositions of high fibrinogen yield and therapeutically effective strength. For example, independent claim 1 specifies that about 95%, or greater, of the total protein present in the composition is fibrinogen, and independent claim 2 specifies that the composition contains less than about 30% of proteins other than fibrinogen. Similarly, independent claim 13 is directed to a reactive therapeutic composition of thrombin and fibrinogen composition. This claim also specifies that about 95%, or greater, of the total protein present in the fibrinogen composition is fibrinogen.

Applicants' claims further specify, in part, that the clottable fibrinogen is obtained from precipitating fibrinogen from a sample of non-human mammalian blood plasma with polyethylene glycol 1000 and reprecipitating the fibrinogen with glycine, wherein precipitation of the fibrinogen with polyethylene glycol is performed only once, such that at least about 90% of the fibrinogen present in the sample is recovered. *See* page 26 of Applicants' specification.

As disclosed in Applicants' specification at page 27, precipitation of fibrinogen with PEG 1000 leads to a cohesive fibrinogen precipitate that is more readily collected, for resuspension, than fibrinogen precipitate resulting from contact with, for example, PEG 8000. Accordingly, use of low molecular weight PEG (such as PEG 1000) facilitates recovery of clottable fibrinogen.

Referring now to the Schwarz reference cited by the Examiner, it is respectfully asserted that this reference does not disclose nor suggest Applicants' presently claimed invention. For example, the tissue adhesive of Schwarz includes fibrinogen in an amount of at least 70 mg/ml (Col. 1, lines 57-61), as recognized by the Examiner at page 3 of the 4/10/02 Action. As distinguished in Applicants' specification at page 4, line 21 continuing to page 5, line 19:

> [t]herapeutic adhesive fibrinogen compositions disclosed [in Schwarz] are stated to require concentrations of fibrinogen of at least about 70 mg/ml (which may again be diluted 1:1 at the treatment site by contact with a thrombin-containing solution).
>
> The present invention relates to fibrinogen-containing compositions that have *surprising clinical (medical) utility* as adhesives, sealants, or hemostatic agents, and that provide therapeutically effective strength at fibrinogen concentrations at the treatment site of, for example, *only about 10 mg/ml. The more dilute and less viscous nature of the therapeutic compositions provided according to the practice of the present invention decreases substantially the time necessary to resuspend such compositions from the lyophilized form, an important advantage in, for example, the hospital emergency room. Filtration of the fibrinogen during processing is also facilitated.*

Thus, the tissue adhesive of Schwarz appears to even teach away from the present invention.

Applicants further respectfully point out that the "capable" wording objected to by the Examiner has been removed in an effort to further clarify the rejected claims, particularly with respect to concentration, as suggested by the Examiner.

It is respectfully asserted that the addition of Tripodi does not cure the shortcomings of Schwartz. Tripodi is directed to a fibrinogen based adhesive. However, in contrast to Applicants' claimed invention, Tripodi recommends the use of PEG-8000 (Page 6). As disclosed in Applicants' specification at page 27, precipitation of fibrinogen with PEG 1000 leads to a cohesive fibrinogen precipitate that is more readily collected, for resuspension, than fibrinogen precipitate resulting

from contact with, for example, PEG 8000. Accordingly, use of low molecular weight PEG (such as PEG 1000) facilitates recovery of clottable fibrinogen. Such clottable fibrinogen is set forth in the present claims.

In view of the foregoing, reconsideration and withdrawal of this rejection is respectfully requested.

All issues raised by the Examiner having been addressed, it is respectfully submitted that the subject application is in condition for allowance.

The Examiner is invited to telephone the undersigned attorney at 212-425-7200 with any questions or comments regarding this Amendment.

Authorization is also hereby given to charge any deficiency in fees in connection with this Amendment to our Deposit Account No. 11-0600.

Also, attached hereto is a Marked-up Version Showing Changes Made By The Present Amendment in accordance with 37 C.F.R. § 1.121.

Respectfully submitted,

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Marked-up Version Showing Changes Made
By The Present Amendment (37 C.F.R. § 1.121)

In the Claims:

Please amend claims 1, 2 and 13, and cancel non-elected claims 18-25 and 27-34 as follows:

1. (Amended) A therapeutic composition effective on contact with thrombin at a site of treatment in a patient as a tissue adhesive, hemostat or sealant, said composition comprising non-autologous, non-single donor mammalian, clottable fibrinogen recovered from a process comprising precipitating fibrinogen from a sample of non-human, mammalian blood plasma with polyethylene glycol 1000 and reprecipitating said fibrinogen with glycine, wherein precipitation of said fibrinogen with polyethylene glycol is performed only once, such that at least about 90% of the fibrinogen present in said sample is recovered, wherein said recovered fibrinogen [is capable of polymerizing] polymerizes when provided in solution at said site at a concentration of about 10 mg/ml thereof or less, to a fibrin network having therapeutically effective strength, and said composition further comprising a sufficient amount of one or more physiologically-compatible solutes such that said composition, if formulated as a lyophilized material, can be reconstituted therefrom at room temperature in sterile water for injection in about 30 minutes or less, at about 25

mg/ml of said fibrinogen; wherein about 95%, or greater, of total protein present in said composition is fibrinogen.

2. (Amended) A therapeutic composition effective on contact with thrombin at a site of treatment in a patient as a tissue adhesive, hemostat or sealant, said composition comprising non-autologous, non-single donor mammalian, clottable fibrinogen recovered from a process comprising precipitating fibrinogen from a sample of non-human, mammalian blood plasma with polyethylene glycol 1000 and reprecipitating said fibrinogen with glycine, wherein precipitation of said fibrinogen with polyethylene glycol is performed only once, such that at least about 90% of the fibrinogen present in said sample is recovered, wherein said recovered fibrinogen [is capable of polymerizing] <u>polymerizes</u> when provided in solution at said site at a concentration of about 30 mg/ml thereof or less, to a fibrin network having therapeutically effective strength, wherein said composition contains less than about 30% (w/w), based on total protein mass present therein, of proteins other than fibrinogen, and said composition further comprises a sufficient amount of one or more low molecular weight physiologically-compatible solutes such that said composition, if formulated as a lyophilized material, can be reconstituted therefrom at room temperature in sterile water for injection in about 30 minutes or less, at about 25 mg/ml of said fibrinogen.

13. (Amended) A reactive therapeutic composition effective on contact at a site of treatment in a patient as a tissue adhesive, hemostat or sealant, said

composition comprising, per milliliter thereof, between about 0.05 and about 500 NIH units of thrombin and also, per milliliter, between about 5 and about 30 mg of a fibrinogen composition wherein clottable fibrinogen is recovered from a process comprising precipitating fibrinogen from a sample of non-human, mammalian blood plasma with polyethylene glycol 1000 and reprecipitating said fibrinogen with glycine, wherein precipitation of said fibrinogen with polyethylene glycol is performed only once, such that at least about 90% of the fibrinogen present in said sample is recovered, said recovered fibrinogen [capable of being polymerized] polymerizes to a fibrin network having therapeutically effective strength, when present at said site at a concentration of about 30 mg/ml or less; wherein about 95%, or greater, of total protein present in said fibrinogen composition is fibrinogen.

Please cancel claims 18-25 without prejudice.

Please cancel claims 27-34 without prejudice.